A method and means for image processing

The present invention relates to methods and means for
image processing and, particularly, though not
exclusively, to the processing of Nuclear Magnetic
Resonance image data.

Dynamic imaging, such as dynamic MR imaging, may involve
the acquisition of a time-series of image data sets in
which each data set is able to represent an image of the
subject fully in 2 or 3 dimensions at one of a series of
successive instants (or brief periods) in time. Dynamic
imaging is often used to record the internal changes in
properties of a stationary subject which are induced by a
controlled change-inducing influence. An example of this
is contrast-enhanced medical MR imaging in which a
"contrast agent" is introduced into a stationary subject
(e.g. a person) which is detectable as an increase in the
image contrast/brightness of those internal parts of the
subject in which the agent is located.

An analysis of the change in image properties (e.g. in
image contrast/brightness), over time, of chosen fixed
points or static regions within the imaged volume of the
subject enables an assessment of the properties of the
chosen fixed points/regions within that imaged volume.

For example, the image analysis procedure in breast
dynamic imaging typically involves localisation of a
lesion within an image of the subject containing a
contrast agent. According to present image analysis
procedures, the pixel value of each pixel within an image
of the subject containing a contrast agent (post-contrast

images) has subtracted from it the pixel value of the corresponding pixel located at the same image point within an image of the same subject taken prior to introduction of the contrast agent thereto (pre-contrast

5   image). The result is a "subtraction image" which ideally includes only the effects of the contrast agent upon the subject.

In many situations the image subject (e.g. region of a

10   body, such as a breast) contains a high content of material (e.g. fat) other than the material of interest which may obscure relevant image features (e.g. lesion shape features) within a post-contrast image. This is especially so in breast-scan images. While the technique

15   of generating subtraction images aims to remove the contribution to, or part of, the image arising from fat (and other materials to which the use of the contrast agent was not directed), this can never be fully achieved due to the fact that materials (especially fat) other

20   than the material of interest may often also be enhanced to a small extent by the presence of a contrast agent. Thus, even a subtraction image is likely to suffer the obscuring effects discussed above arising from undesired image contrast enhancement.

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Analysis of lesion shape within an image and of the pattern of enhancement due to contrast agent uptake may make a valuable contribution to diagnosis. The analysis of lesion shape can only be considered reliable in cases

30   where the tumour extent is properly segmented within the image being studied. The "traditional" approach to this problem is manual segmentation of the tumour region within subtraction images (e.g. by a radiologist). Even if the shape obscuring tissue is not enhancing, it cannot

be eliminated using the subtraction technique because of noise present in the pre-contrast and/or post-contrast image data. As a result the tumour-outlining contour so produced is not always well defined.

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Moreover, merely segmenting the outlining image contour of a tumour image may not be satisfactory/sufficient if the tumour in question has a heterogeneous structure, which is not clearly seen on a subtracted image. As a

10   result the pattern of contrast enhancement is not always clearly seen on the subtraction image. Furthermore, a subtraction image alone does not always permit one to discriminate between tumour and other enhancing tissues, e.g. blood vessels.

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The present invention aims to overcome at least some of the above deficiencies of the prior art.

The present invention, at its most general, proposes to

20   provide a method and/or means enabling one to identify in an image, being one of a time-sequence of images recording induced changes in pixel values of successive images of a subject (such as post-contrast dynamic images), the contribution to the image arising from the

25   presence within the image subject of a specified material/tissue (such non-enhancing and/or low-enhancing material, e.g. fat). This identification is proposed to be done using a statistical measure derived from the dynamic data (e.g. pixel value changes due to contrast

30   agent uptake) taken from a plurality of the separate images forming the time-sequence.

In the case of a time-sequence of images recording the development of contrast-enhancement in a subject, this is

preferably done in respect of individual image pixels (or "voxels" in a 3D image) from information contained in the pixel intensity data recording the contrast enhancement of the subject at a point or pixel location therein.

5   Thus, the statistical measure is most preferably derived according to the variation over time of the pixel intensity at an individual image pixel location (i.e. the "uptake curves" representing contrast enhancement due to contrast agent uptake over time at a given imaged point).

10

The pixel intensity of a given pixel changes over time either predominantly in response to a deliberate induced effect (e.g. the presence of a contrast enhancing agent) at the location within the subject represented by the

15   pixel,   and/or   due   to   image   noise.   Different material/tissue types respond differently to the presence of a contrast enhancing agent and the present invention proposes a method and means for utilising this fact in identifying different materials within the image of a

20   subject, using a statistical measure of the induced image pixel value changes (over time) which has been found to be tissue-specific.

The invention is particularly suited to identifying fat

25   and/or fatty tissues within the image of a subject and it has been found that the statistical measures described herein are particularly well suited to identifying the present of such tissues specifically.

30   It is to be understood that the present invention is not limited to the processing of Nuclear Magnetic Resonance image data and is applicable to the processing of image data acquired via other means and in respect of any subject.

Accordingly, in a first of its aspects, the present
invention may provide a method of processing a time-
sequence of separate image data sets which records
5   induced changes in pixel values of successive images of a
subject, each set comprising a plurality of image data
items which each represent the location of an image pixel
of the image subject according to a common reference
frame within which the subject is located, the method
10   including the steps of:

       (a) selecting from each of a plurality of the
separate image data sets an image data item which
represents an image pixel located at the same fixed image
pixel location, thereby to generate a time-domain image
15   data set preferably containing only image data items
which represent an image pixel at the same said pixel
location;

       (b) determining according to a measure (e.g.
predetermined) of said induced changes or differences as
20   between the (preferably all of the) pixel values of the
image·data items of the time-domain image data set
whether the image data items thereof are associated with
the presence of a specified material (most preferably a
tissue, e.g. fat) within the image subject.

25

There may then follow an additional step (c), following
step (b), of identifying or classifying the image data
items of the time-domain image data set as being
unsuitable for use in the generation of an image of the
30   subject if they are identified in step (b) as being
associated with the presence of the specified material or
tissue (e.g. fat) within the image subject and if the
specified material or tissue is of a type which it is not
desired to be included within the image of the subject.

Otherwise, the image data items in question may be
identified/classified as being suitable for use in image
generation of the subject.

5   Thus, the time-domain image data set contains information
regarding exclusively the image pixels representing the
same location within the common reference frame of each
of the plurality of successive images in the time-
sequence of images. Most preferably each and all of the
10   data items within the time-domain image data set are
employed in determining whether or not the image data
items thereof correspond with the specified
material/tissue (e.g. in determining the measure). For
example, the measure may be a measure of, or be sensitive
15   to, differences between each pixel value in the time-
domain image data set as compared to each other such
pixel value. The result is that the measure is then
sensitive to the general dispersion of pixel values
forming the time-domain image data set, and can provide a
20   measure of how similar/different the image pixel values
are collectively.

By analysing the information contained in this dynamic
time-domain image data set, one is able to derive
25   information in respect of any one of the plurality of
separate image data sets within the time-sequence which
would not be derivable from that one image data set alone
- namely, whether a pixel value therein results from a
specified material or tissue (e.g. fat or fatty tissues)
30   within the image subject, or otherwise.

The measure of the induced effect may be any one of a
number of measures, which enable, from an analysis of the
time-development of the intensity value of a pixel at the

same location within each of the separate images in the
time-sequence, whether that development arose
predominantly due to a specific material or tissue (e.g.
fat). Such measures as would be readily apparent to the
5   skilled person may be employed according to the present
invention. However, the measures described herein have
been found to be specifically suited to identifying the
presence of fat and fatty tissues as discussed below.

10   Where the pixel location of an image is non-responsive or
only weakly responsive to an inducement to changes in its
pixel value, when the imaged subject is exposed to a
deliberate change-inducing influence or agent, the value
of the pixel at that location is likely to be the same
15   (or similar) in each of the images within the time-
sequence. Conversely, if the location is strongly
responsive to such inducements to changes in its pixel
value, the value of the pixel at that location is likely
to change significantly over time within the time
20   sequence.

Accordingly, the measure is most preferably defined
according to a measure of the dispersion of, or
differences between, the values of pixel intensity
25   associated with the image data items within the time-
domain image data set. If only a small degree of
difference (as between values) in such pixel intensity
values exists when considering all pixel values
represented within the time-domain image data set, this
30   amounts to a small dispersion in pixel intensity values
and suggests the observed dispersion results from the
pixel values representing tissue/material (e.g. fat)
within the imaged subject which is non-responsive or only

weakly responsive to the inducements to change. The
image data items of the time-domain image data set may be
so classified and may be identified as being not suitable
for use in the generation of an image of the subject.

5 Conversely, large values of dispersion suggest the
observed dispersion arises from materials strongly
responsive to the inducement to change and may be so
classified. These image data items of the time-domain
image may also be classified as being suitable for use in

10 the generation of an image of the subject.

Preferably, the image data items of the time-domain image
are determined as being associated with the presence
within the image subject of the specified material if the

15 measure exceeds a predetermined threshold value.
Preferably, the predetermined threshold is a value of the
measure of dispersion in the values of pixel intensity
associated with the image data items within the time-
domain image data set.

20

For example, the measure (e.g. of dispersion) may be
determined according to the extent to which the pixel
values represented by the image data items of the time-
domain image data set differ from equality (i.e. the

25 extent to which they do not all share the same value).
To this extent, the measure (e.g. of dispersion) may be
determined according to the degree to which a time-domain
image vector differs from an identity vector in the same
vector space. Each vector component of the time-domain

30 image vector is preferably represented by a unique image
data item of the time-domain image data set. Preferably,
the array of vector components is arranged in time-
sequence. All vector components of the identity vector
share the same value (preferably, the value 1 (one)).

The degree of difference (and therefore the measure e.g.
of dispersion) may be the angle subtended by the time-
domain image vector with respect to the identity vector.
Indeed, the measure of dispersion may be determined

5   according to any suitable property of the time-domain
vector in vector space. Preferably, the property in
question is a property of the vector as a whole (e.g. its
angle relative to another as above).

10   For example, step (b) of the method of the present
invention in its first aspect may include:
        forming a time-domain image vector wherein each
image data item of the time-domain image data set
represents a separate vector component of the time-domain

15   image vector (e.g. an array of vector components arranged
in the time-sequence to form the vector); and determining
the measure according to a property of the time-domain
image vector.

20   For example, determining the measure could include
determining the angle (α) subtended by the time-domain
image vector with respect to the identity vector
(preferably in the vector space of the time-domain image
vector); and, employing the angle (α) as the measure.

25   The predetermined threshold value discussed herein is
then preferably a predetermined value of the measure.

Alternatively, the measure e.g. of dispersion in the
values of pixel intensity associated with the image data

30   items within the time-domain image data set may be
determined according to a property or properties of one
or more of the principal components of the time-domain
image vector determined according to a principal
component decomposition of the time-domain image vector.

It has been found that the value of the second principal
component (that is, the principal component associated
with the second largest eigenvalue of the Principal

5   Component Analysis (PCA)) provides a reliable measure of
the dispersion in the values of pixel intensity
associated with the image data items within the time-
domain image data set. Preferably, the predetermined
threshold is a predetermined value of the second

10   principal component of the time-domain image vector.
Preferably, the predetermined threshold value is exceeded
if the value of the second principal component is greater
than zero.

15   For example, step (b) may include:
           forming a time-domain image vector wherein each
image data item of the time-domain image data set
represents a separate vector component of (e.g. an array
of vector components arranged in the time-sequence to

20   form...) the time-domain image vector;
           determining the second principal component of the
time-domain image vector; and,
           employing the value of the second principal
component as the measure. The predetermined threshold

25   discussed herein value may then preferably be a
predetermined value of the measure.

Where step (b) includes the calculation of the angle (α)
the predetermined threshold value may be deemed to be

30   exceeded if the angle (α) is less than a threshold angle
value (α_0). The threshold value (α_0) may be arbitrarily
set by the user, but is preferably determined according
to the distribution of the angular values (α) of the
time-domain image vectors associated with a plurality of

(preferably all of) the image pixel locations represented in the time-sequence of data sets.

The method may include:

5   repeating step (a) in respect of a plurality of image data items thereby to generate a corresponding plurality of time-domain image data sets; and

       forming a corresponding plurality of time-domain image vectors with each image data item of a given time-

10   domain image data set representing a separate vector component of (e.g. an array of vector components arranged in the time-sequence to form...) the given time-domain image vector; then

       determining the angle subtended by each of the time-

15   domain image vectors with respect to the identity vector e.g. in the vector space of the time-domain image vector; and,

       determining from the distribution of the values of the angles (preferably the values of the natural

20   logarithm of the angles) of all of the time-domain vectors the portion of the angular distribution arising mainly, predominantly, or substantially only from the presence of the specified material within the image subject. The predetermined threshold value may then be

25   deemed to be exceeded if the angle subtended by the time-domain image vector falls within, or contributes to, the portion of the angular distribution arising from the specified tissue/material (e.g. fat).

30   Preferably, the threshold angle value (α_0) is the angular value which demarcates the portion of the angular distribution arising mainly, predominantly, or substantially only from the specified tissue/material from the other portion(s) of the angular distribution.

For example, the portion of the angular distribution
arising mainly, predominantly, or substantially only from
the specified tissue/material may be determined according
to a Normal Distribution having distribution parameters
5   which cause it to most closely correspond with a portion
of the angular distribution. Demarcation may be
performed graphically/visually, or may be performed
analytically and automatically using, for example, the
well-known ROC technique in a manner such as would be
10   readily apparent to the skilled person ("Receiver
Operating Characteristics": see D J Fink and D
Christiansen, Electronic Engineer's Handbook, McGraw-
Hill, 3rd edition (1989), section 25, pp119-120).

15   The method of processing image data, in its first aspect,
preferably includes the additional step of:
     (d) replacing by a value of zero the pixel value of
each image data item of each of the plurality of the
separate image data sets identified as being unsuitable
20   for use in the generation of an image of the subject.
In this way, separate image data sets of the time-
sequence may be processed to remove tissue/material-
specific pixels values therefrom leaving unchanged only
those pixels which have been processed only if they have
25   been deemed suitable for use in image formation.

Furthermore, the removal of noise from the image data may
be achieved by decomposing according to a principal value
decomposition the/each time-domain image vector which has
30   been deemed suitable for use in image formation, and
discarding from the decomposed vector those principal
components which are deemed to arise predominantly from
random causes.

For example, the method may also include representing the
time-domain image vector in terms of a principal
component decomposition thereof employing all principal
component vectors and corresponding principal component

5   values thereof except: those principal component values
thereof not exceeding a predetermined magnitude; and,
       replacing by a value determined according to the
principal component decomposition the pixel value of each
image data item of each of the plurality of the separate

10   image data sets identified as being suitable for use in
the generation of an image of the subject.

However, it has also been found that the first (largest)
principal component of a time-domain image vector

15   generally corresponds to the image data common to all
images of the time-sequence. Thus, in the case where the
time-sequence records contrast enhancement beginning with
a pre-contrast image, the first principal component of
each time-domain image vector of the sequence

20   approximately represents the information contained within
the pre-contrast image data set, that being the first set
within the time-sequence. Subtraction of this
information from the time-domain image vectors will
result in the maximisation of the differences between

25   different time-domain image vectors (e.g. uptake curves)
by removing the information which is common to all time-
domain image vectors (e.g. uptake curves). The term
"subtraction" is to be understand to refer to the
reconstruction of a vector using its principal components

30   except (i.e. omitting) its 1st principal component.

Thus, the method may also include representing the time-
domain image vector in terms of a principal component
decomposition thereof employing all principal component

vectors and corresponding principal component values
thereof except: those principal component values thereof
not exceeding a predetermined magnitude; and/or the
largest principal component value thereof; and,

5   replacing by a value determined according to the
principal component decomposition the pixel value of each
image data item of each of the plurality of the separate
image data sets identified as being suitable for use in
the generation of an image of the subject.

10

Preferably, the method of processing according to the
invention in its first aspect, includes repeating steps
(a) and (b), or steps (a) to (c), (including any of the
preferable/alternative features described above) in

15 respect of pixels at each pixel location represented
within the time-sequence of separate image data sets.
Thus, preferably all image pixels are processed as above.
Of course, the present invention may provide a method of
forming an image from image data comprised in the time-

20 sequence of separate image data sets having been
processed according to the invention in its first aspect
(including any of the preferable/alternative features
described above).

25 It is to be understood that the present invention may
provide means arranged to, or suitable for, the
implementation of the invention in its first aspect.
Accordingly, it is to be understood that the present
invention encompasses such means.

30

For example, in a second of its aspects, the present
invention may provide an image processing means for
processing a time-sequence of separate image data sets
which record induced changes in pixel values of

successive images of a subject, each set comprising a
plurality of image data items which each represent the
location of an image pixel of the image subject according
to a common reference frame within which the subject is
5   located, the image processing means including:

         (a) selection means for selecting from each of a
plurality of the separate image data sets an image data
item which represents an image pixel located at the same
fixed image pixel location, thereby to generate a time-
10   domain image data set preferably containing only image
data items which represent an image pixel at the same
said image pixel location;

         (b) decision means for determining according to a
measure of said induced changes as between preferably all
15   of the pixel values of the image data items of the time-
domain image data set whether the image data items
thereof are associated with the presence of a specified
tissue/material within the image subject.

20   The apparatus may also include:
     (c) identifying means arranged to identify or classify
the image data items of the time-domain image data set as
being unsuitable for use in the generation of an image of
the subject if they are identified by said decision means
25   (b) as being associated with the presence of the
specified material within the image subject and if the
specified material is of a type which it is not desired
to be included within the image of the subject. The
identifying means may be arranged to otherwise identify
30   the image data items in question as being suitable for
use in image generation of the subject.

     Preferably, the decision means is arranged to determine
that the image data items of the time-domain image are

associated with the specified material if the measure
exceeds a predetermined threshold value. Preferably, the
predetermined threshold is a predetermined value of the
measure of dispersion in the values of pixel intensity
5   associated with the image data items within the time-
domain image data set.

To this extent, the measure e.g. of dispersion may be
determined according to the degree to which a time-domain
10   image vector differs from an identity vector in the same
.vector space, wherein each vector component of the time-
domain image vector is represented by a unique image data
item of the time-domain image data set (e.g. the array of
vector components being arranged in time-sequence), and
15   all vector component of the identity vector share the
same value. The degree of difference (and therefore the
measure of dispersion) may be the angle subtended by the
time-domain image vector with respect to the identity
vector.
20

The decision means may include:
        vector means for forming a time-domain image vector
wherein each image data item of the time-domain image
data set represents a separate vector component of the
25   time-domain image vector (e.g. an array of vector
components arranged in the time-sequence to form the
vector);
        angle determining means for determining the angle
(α) subtended by the time-domain image vector with
30   respect to the identity vector e.g. in the vector space
of the time-domain image vector.
        The decision means is preferably arranged to employ
the angle (α) as the measure, and the predetermined

threshold value is preferably a predetermined value of
the predetermined measure.

Alternatively, or additionally, the decision means may
5   include:
        vector means for forming a time-domain image vector
wherein each image data item of the time-domain image
data set represents a separate vector component of (e.g.
an array of vector components arranged in the time-
10   sequence) the time-domain image vector;
        principal component means for determining the second
principal component of the time-domain image vector;
        wherein the decision means is arranged to employ the
value of the second principal component as the measure.
15   The predetermined threshold value is then preferably a
predetermined value of the measure. Preferably, the
predetermined threshold is exceeded if value of the
second principal component is greater than zero.

20   Where the decision means employs the angle (α), the
predetermined threshold value may be deemed to be
exceeded if the angle (α) is less than a threshold angle
value (α_0).

25   The selection means is preferably arranged to generate in
respect of a plurality of image data items a
corresponding plurality of time-domain image data sets;
        the vector means is preferably arranged to form a
corresponding plurality of time-domain image vectors with
30   each image data item of a given time-domain image data
set representing a separate vector component of (e.g. an
array of vector components arranged in the time-sequence)
the given time-domain image vector.

The angle determining means is preferably arranged to
determine the angle subtended by each of the time-domain
image vectors with respect to the identity vector in the
vector space of the time-domain image vector; and,

5   the decision means is preferably arranged to
determine from the distribution of the values of the
angles (preferably the values of the natural logarithm of
the angles) of all of the time-domain vectors the portion
of the angular distribution arising predominantly,

10   mainly, or substantially only from the presence of the
specified material within the image subject. The
predetermined threshold value may then be deemed to be
exceeded if the angle subtended by the time-domain image
vector falls within the portion of the angular

15   distribution arising from the specified material.

Preferably, the threshold angle value (α_0) is the angular
value which demarcates the portion of the angular
distribution arising substantially only from the

20   specified material from the other portion(s) of the
angular distribution.

The decision means may be arranged to determine the
portion of the angular distribution arising substantially

25   only from the specified material according to a Normal
Distribution having distribution parameters which cause
it to most closely correspond with a portion of the
angular distribution.

30   The image processing means of the present invention, in
its second aspect, preferably includes:
        (d) data modifying means arranged to replace by a
value of zero the pixel value of each image data item of
each of the plurality of the separate image data sets

identified by the identifying means (c) as being
unsuitable for use in the generation of an image of the
subject.

5   The principal component means is preferably arranged to
represent the time-domain image vector in terms of a
principal component decomposition thereof employing all
principal component vectors and corresponding principal
component values thereof except: the largest principal
10 component value thereof; and those principal component
values thereof not exceeding a predetermined magnitude.

The image processing means preferably further includes
data modifying means arranged to replace by a value
15 determined according to the principal component
decomposition the pixel value of each image data item of
each of the plurality of the separate image data sets
identified as being suitable for use in the generation of
an image of the subject.
20

The image processing means of the present invention,
according to its second aspect is preferably arranged to
process each pixel of each of the time-sequence of
separate image data sets.
25

The image processing means preferably includes image
forming means for forming an image from image data
comprised in the time-sequence of separate image data
sets having been processed by the image processing means
30 according to the invention in its second aspect
(including any of the aforementioned
preferable/alternative features thereof).

The invention may provide computer means programmed to
perform the method according to the invention in its
first aspect (including any of the aforementioned
preferable/alternative features thereof). The invention
5   may provide a computer program product containing a
computer program for performing the method according to
the invention in its first aspect (including any of the
aforementioned preferable/alternative features thereof).
The invention may provide a computer program for
10 performing the method according to the invention in its
first aspect (including any of the aforementioned
preferable/alternative features thereof). The invention
may provide an image generated according to the method of
the invention in its first aspect (including any of the
15 aforementioned preferable/alternative features thereof).

The invention shall now be described in terms of the
following non-limiting examples with reference to the
accompanying drawings in which:
20   Figure 1 illustrates the distribution of the natural
logarithm of the value of the angle subtended by the
time-domain image vectors of each image pixel location of
a time-sequence of images relative to the identity vector
in the image space of the time-domain image vectors;
25   Figure 2 illustrates a decomposition of the
distribution illustrated in figure 1 into a Normal
component most closely corresponding with a Normal
Distribution, and a residual component being the
difference between the Normal component and the
30 distribution of figure 1;
        Figure 3 illustrates a decomposition of the
distribution illustrated in figure 1 into two fractions
("fat" and "non fat") discriminated using the value of

the second principal component with threshold value equal
to zero;

Figure 4 illustrates the effects upon the
distribution of figure 1 of not removing background noise
5   from the distribution (such removal having occurred in
the distribution of figure 1);

Figure 5(a) illustrates a sequence of post-contrast
images processed according to the present invention
(post-contrast time is incrementing from left to right);
10   Figure 5(b) illustrates a sequence of post-contrast
subtraction images according to known methods;

Figure 5(c) illustrates an enlarged first image of
the sequence illustrated by figure 5(a)

Figure 6(a) illustrates an image processed according
15   to the present invention;

Figure 6(b) illustrates a post-contrast subtraction
image according to known methods;

Figure 7 illustrates a histogram of first principal
components;
20   Figure 8 illustrates a normalised uptake curve, a
time-development of a first principal component of an
uptake vector, and a linear uptake model;

Figure 9a to 9f illustrate a subject image and
comparison images subject to different image processing;
25   Figures 10a to 10d illustrate a subject image and
comparison images subject to different image processing;

Figures 11a to 11c illustrate a sequence of
processed images and a high-resolution comparison image.

30 In the following, the invention shall be illustrated in
terms of the processing of a dynamic image data set
recording contrast enhancement in a subject containing a
high fat content. The invention shall be describes in

its application as a method and means of identifying fat
or fatty tissues within an NMR image.

Consider a time-sequence of M separate image datasets
5   each of which contains image data elements acquired by
Magnetic Resonance Imaging of a subject immediately
before and subsequent to application of an image contrast
enhancing agent, and representing the imaged subject in
three dimensions (i.e. a volume image). Each volume
10   image is represented as a stack of two-dimensional image
frames with lattice dimensions N_x, N_y, N_z (respectively
number of columns and rows in a frame, and a stack
length), and total number of image pixels (or "voxels"
for a volume image) is $N = N_x \times N_y \times N_z$.
15

Let $\mathbf{Y}_i = \left(y_{i,1}, \ldots, y_{i,M} \right)$, i = 1, ..., N be a time-domain image data
set (representing a contrast enhancement agent uptake
vector, i.e. the vector representation of an uptake curve
of a single voxel) of a single voxel at a fixed image
20   point "i" common to each of the M separate image data
sets within the sequence. The time-domain image data set
is expressed as a vector in M-dimensional Euclidean space
wherein each image data item of the time-domain image
data set represents a separate vector component of an
25   array of vector components arranged in said time-sequence
to form the time-domain image vector $\mathbf{Y}_i = \left(y_{i,1}, \ldots, y_{i,M} \right)$.

One may distinguish between non- and low-enhancing
tissues, such as fat, and the tissues enhancing to a high
30   extent.

We assume that each uptake vector belongs to a certain
class corresponding to a tissue of specific kind. The

dispersion/differences in image pixel values of corresponded temporal points of the time-domain image vectors (uptake vectors) from the same class are only due to the random noise. It follows that

$$y_{i,j} \propto Norm(\mu_{k,j}, \sigma^2), \qquad i \in \Lambda_k$$

Where Λ_k is a set of uptake vectors that build the kth cluster in the Euclidean space within which the time-domain image vectors are defined. The quantity $\mu_{k,j}$ is the expected value of the jth value (temporal point) of an uptake vector that belongs to the kth cluster, and the quantity σ is the standard deviation of the random noise which may, for simplicity, be assumed to be the same for all the dynamic images (this assumption is, however, not necessary).

We shall base our classification on the following model. The dispersion of values of the components ($y_{i,j}$) of an individual time-domain image vector $Y_i = (y_{i,1}, ..., y_{i,M})$ (uptake vector) can be modelled by two factors:

(1)   contrast enhancement, being induced and due to a deliberate effect, increases the dispersion of the expected values $\mu_{k,1}, ..., \mu_{k,M}$ of the corresponded cluster; and,

(2)   random noise.

For a cluster representing low enhancing tissue, the difference between the temporal points of an uptake curve is mostly due to noise and so the dispersion of the expectation values $\mu_{k,1}, ..., \mu_{k,M}$ is small.

It follows that for non-enhancing and low-enhancing tissues the dispersion should be less than is observed in a significantly contrast-enhancing tissue, since the

5   tissue is not subject to a deliberate or significant contrast-enhancing effect, or if there is any such effect it relatively small.

To establish a measure of the enhancement effect, one may

10   find a measure of the dispersion of $\mu_{k,1},...,\mu_{k,M}$. This may be done using the time-domain vector, $\mathbf{Y}_i = (y_{i,1},...,y_{i,M})$, and the idem (or "identity") vector, $\mathbf{1}_{1\times M} = \underbrace{(1,...,1)}_{M}$ as follows.

Considering the uptake curves as vectors in M-dimensional Euclidean space (as mentioned above), the smaller the

15   dispersion of the expectation values $\mu_{k,1},...,\mu_{k,M}$, the closer to the idem vector will lay the vectors of the cluster Λ_k. Thus, the angle (α) subtended by a given time-domain image vector with respect to the idem vector in the vector space of the time-domain image vector is

20   determined and employed as a measure of the degree of dispersion present within that vector. This measure reflects both the enhancement effect and the random noise. The effect of noise should be taken into account. One should find a threshold value α_0. Should an uptake

25   vector posses value $\alpha > \alpha_0$, the uptake vector reflects significant enhancement. Statistically this is equivalent to testing the hypothesis that the vector represents tissue, possessing enhancement bigger than the non- or low responsive material (e.g. fat) Later we describe how

30   to determine the threshold analysing the distribution of the statistics (α).

Assuming that the values of α are small:

$$\alpha_i \approx tg(\alpha_i) = \frac{\sqrt{\frac{1}{M}\sum_{j=1}^{M}(y_{i,j} - \bar{y}_{i,\bullet})^2}}{\bar{y}_{i,\bullet}} \tag{1}$$

Where $\bar{y}_{i,\bullet} = \frac{1}{M}\sum_{j=1}^{M} y_{i,j}$ is the average of the temporal points of

5   the time-domain vector (uptake vector).

The angle (α) is determined in respect of all time-domain
image vectors (uptake vectors) of all image pixel points
of the image volume thereby to generate a corresponding

10   plurality of such angles. It can be straightforward
proven mathematically that the values of α will be
approximately log-normally distributed. Each cluster, Λ_k,
will possess its own distribution, so for the whole
volume one shall have a mixed distribution.

15

One may determine from the distribution of the values of
the angles of all of said time-domain vectors the portion
of the angular distribution arising substantially only
from the presence within the image subject of a specified

20   low-enhancing tissue (e.g. fat). Once this specified
portion has been determined, one may then determine that
the contribution to the pixel values of the image data
items of a given time-domain image vector (uptake vector)
arising from the specified material exceeds a

25   predetermined threshold value if the angle α subtended by
that time-domain image vector falls within the specified
portion of the angular distribution.

Figure 1 shows an example of the distribution of the

30   values of ln(α) for a dynamic breast MR measurement (the

solid line). One can see that this is a mixed distribution. One can identify a cluster corresponding to the small values of α (shown by the fitted Normal Distribution (Gaussian) curve - the dashed line). The

5   identified cluster is closer to the idem vector in terms of α, i.e. possessing small enhancement effect. It also represents statistically the most significant and uniform fraction of the population. One may conclude that this cluster represents tissue not significantly responsive to

10   contrast agent, such as fat (at least), within the imaged subject. In general, this cluster represents a tissue that is not highly responsive to the contrast agent and which is not the tissue of interest to which the use of the contrast agent was directed. Hereafter, we shall

15   refer to the identified cluster as a "cluster of fat" to simplify the discussion.

Fitting the normal distribution curve (the dashed line of figure 1) to the fat cluster, the whole angular

20   distribution (dotted curve of figure 2) can be decomposed into normal fraction (the solid curve of figure 2) representing fat and the residual fraction shown as the dashed curve at the right in figure 2. The residual fraction is a mixed distribution corresponding to the

25   enhancing tissues in the imaged subject. The significantly enhancing tissues are much more heterogeneous than fat, and therefore fall in a number of small overlapping clusters. Using the decomposed distribution one can find the optimal threshold, α_0,

30   discriminating between normal (fat) and residual populations using for example ROC technique [DJ Fink, D. Christiansen (editors), Electronics Engineers' Handbook, McGraw-Hill, 3rd edition, (1989): section 25 pp. 119-120].

Alternatively, one may wish to select a conservative threshold that discriminates only fat tissue without risk of loss of any valuable information. It is easy to see on figure 2 that the threshold corresponds to $\ln(\alpha) \approx -2.8$. The suppression of image effects caused by fat is done by replacing by a zero-vector the time-domain image vectors (uptake vectors) $\mathbf{Y}_i = (y_{i,1},...,y_{i,M})$ in the time-sequence of separate image data sets (the matrix D below) which possess a value of the angle $\alpha < \alpha_0$ (i.e. replacement: $\mathbf{Y}_i \rightarrow (0,...,0)$).

Alternatively, or additionally, the threshold may be determined and applied via a decomposition of the time-domain image vectors via a Principal Component Analysis (PCA) as follows.

Let D be a dynamic image matrix those columns are separates time-domain image vectors (uptake vectors) $\mathbf{Y}_i = (y_{i,1},...,y_{i,M})$ for respective separates image pixel locations "i", and each row is formed from the complete contents of successive of the M separate datasets of the time-sequence, as follows

$$D = \begin{bmatrix} y_{1,1} & \cdots & y_{N,1} \\ \vdots & \ddots & \vdots \\ y_{1,M} & \cdots & y_{N,M} \end{bmatrix}$$

Let $p_j = (p_1,...,p_M)$ be the jth principal component (PC) vector and is the ith column in P.

The value

$$Z_{j,i} = (p_j)'Y_i = \sum_{k=1}^{M} p_{j,k} \cdot y_{i,k} ; \qquad j = 1, \dots, M ; \quad i = 1, \dots, N$$

is the value of the jth principle component of ith time-domain image vector (uptake vector).

The order of the principal component vectors in P depends upon the order of the corresponded eigenvalues (λ_k) thereof, such that $\lambda_1 > \lambda_2 > \dots > \lambda_M$.

It has been found that second principal component is associated with the statistical measure (α), and that these two quantities possess a strong negative correlation. Analysis of regression of the correlation of these two quantities has demonstrated that the value of the second principal component $Z_{2,i} = 0$ approximates the value of the threshold α_0. It follows that if $Z_{2,i} > 0$ then the vector Y_i belongs to the "fat cluster"; otherwise the vector Y_i represents significantly enhancing tissue. (In other words, one may say that the above described "fat cluster" falls on the positive extent of the 2nd principal component.) In effect, the 2nd principle component is a statistical measure of enhancement equivalent to α. It should be understood that alternatives to the use of $Z_{2,i} = 0$ as a threshold value (of 2nd principal component) could in principle be used. Figure 3 shows distributions of $\ln(\alpha)$ for populations classified as "fat" and "non-fat" using the described above PCA approach. One can see that the result coincides very well with the aforementioned conservative threshold technique illustrated in figure 2 (the whole distribution and the Gaussian distribution are also shown for comparison – not normalised).

It should be noted that if the aforementioned angular distribution method (α statistics) is employed, background noise (i.e. noise of empty background

5   surrounding the imaged subject) may obscure the optimal threshold, and therefore is preferably removed.

Figure 4 illustrates the effects upon the distribution of figure 1 of not removing background noise (the solid line

10   of figure 4) from the distribution (such removal having occurred in the distribution of figure 1, reproduced as the dashed line in figure 4). However, one can see from figure 4 that the background noise overlaps mainly with the significantly enhancing tissues. The PCA approach is

15   robust to the background noise.

The present invention may also permit as estimation of tissue-specific contrast enhancement effects as follows.

20   One may describe the time-domain image vector (uptake vector data) using the following linear model

$$\mathbf{Y}_i = B_i \mathbf{b} + H_i \mathbf{h}_k + \varepsilon_i \,, \qquad i \in \Lambda_k \,, \qquad k = 1,2,\dots \qquad (2)$$

25   The first term in eq. 2 is a baseline term. The second term describes the specific effect of cluster Λ_k, such that the vector $(B_i \mathbf{b} + H_i \mathbf{h}_k)$ is collinear with the centroid vector of the kth cluster, where $\mathbf{\mu}_k = (\mu_{k,1}, \dots, \mu_{k,2})$ is the centroid vector whose components are the expectation

30   values $\mu_{k,1}, \dots, \mu_{k,2}$. The last term, ε_i, is the residual vector. The vectors $\mathbf{b}, \mathbf{h}_k$ are unit vectors. It is also required that $\mathbf{b} \perp \mathbf{h}_k \perp \varepsilon_i$ for all i,k. It follows

straightforwardly from the definition of the model that the residual term contains only random noise. Indeed, the random noise is defined as $Y_i - \mu_k$. According to the above discussion, $\varepsilon_i \perp \mu_k$ and, therefore, contains only the component of random noise that is orthogonal to μ_k. The complimentary component of noise (i.e. one collinear with μ_k) is spread across the first and second Principal Components (largest and next-largest) of the time-domain image vector (i.e. the first two terms of equation (3) below).

Existing subtraction imaging techniques define a baseline term as $Y_{i,1}\mathbf{1}$, where $Y_{i,1}$ is the first, pre-contrast point of the uptake vector Y_i and $\mathbf{1}$ is the identity vector. These existing techniques estimate the enhancement effect merely as $Y_i - Y_{i,1}\mathbf{1}$, thereby leaving the noise "inside" the image data.

Compare the equation (2) with the following PCA decomposition of Y:

$$Y_i = \sum_{n=1}^{M} Z_{n,i} \mathbf{p}_n \ , \qquad \mathbf{p}_1 \perp \dots \perp \mathbf{p}_M \tag{3}$$

The PCA decomposition is a generic linear model of the data where the meaning of each particular term is unknown. However, by postulating equivalence of equation (2) and equation (3) one may assume that:

(1)   the first Principal Component of the series in equation (3), namely the quantity $Z_{1,i}\ \mathbf{p}_1$, is a "baseline" term;

(2)   a few mid-Components describe the specific enhancement effect; and,

(3) the remaining Principal Components represents the noise which may be discarded from the PCA representation of Y_i .

Any suitable methods, such as would be readily apparent to the skilled person, may be employed to determine the most suitable value for the cut-off number $m < \dot{M}$ being the value such that each jth $(j > m)$ principal component can be deemed to contain noise and can be "safely" discarded.

Thus the specific tissue effect (arising from significantly enhancing tissues) can be estimated using the following equation

$$Y^*_i = H_i \; h \; = \sum_{k=2}^{m} z_{k,i} \; p_k \qquad\qquad (4)$$

In effect this is subtraction of the baseline and residual terms of equation (2). Subtraction of this information from the time-domain image vectors will result in minimisation of the redundant information in the image vectors such that those vectors, and the information within them, therefore, represent substantially only the effects specific to tissue enhancement post-contrast.

Thus, the method of image processing may also include representing the time-domain image vector in terms of a principal component decomposition thereof employing all principal component vectors and corresponding principal component values thereof except: those principal component values thereof not exceeding a predetermined

magnitude; and/or the largest principal component value
thereof; and,

        replacing by a value determined according to the
principal component decomposition of the pixel value of
5   each image data item of each of the plurality of the
separate image data sets identified as being suitable for
use in the generation of an image of the subject.

The invention, in a preferred embodiment, provides a
10 method of processing a time-sequence of separate image
data sets (each being either 2D or 3D) which records
development of contrast enhancement in an imaged subject
into which a contrast-enhancing agent has been
introduced, the method containing some or all of the
15 following steps:

1. PCA decomposition of the time-domain vector for each
   pixel location within the time-sequence of separate
   image data sets; followed by,

2. Suppression of image noise due to the random (and
20   low-enhancing) effects (e.g. of fat) within an
   imaged subject as described above; followed by,

3. Estimation the specific enhancement effect by
   representing each time-domain image vector according
   to equation (4) (and optionally, the data can be de-
25   noised removing a few last terms in the PCA series
   after estimation of the noise cut-off term number
   m).

It is to be understood that the present invention may
30 provide means arranged to, or suitable for, the
implementation of the image processing method of the
invention. Accordingly, it is to be understood that the
present invention encompasses such means.

The image processing may be performed on any suitable
image processing means (e.g. a computer work station)
which preferably includes image forming means for forming
an image from image data having been processed by the
5   image processing means according to the invention.

The invention may provide a computer program product
(e.g. computer disk or other means for carrying/storing a
computer program readable by a computer) containing a
10   computer program for performing the processing method.
The invention may provide a computer program for
performing the method according to the invention.

Figure 5(a) shows the sequence of post-contrast images
15   resulted from using the suggested approach. The
background grey colour in each image outlines eliminated
fatty tissue. The first image of the sequence on the left
is a first post-injection image. Rest of the images are
ordered according to their acquisition times from left to
20   right. The image of the same subject generated according
to known image subtraction techniques, and produced using
the same sequence of datasets as that used for figure
5(a), is shown for comparison on figure 5(b). The time-
sequence of datasets used for the example consists of
25   seven image volumes: two pre- and five post-contrast,
performed after administration of Gd-DTPA. Temporal
resolution was 90 sec. The data sets were acquired using
3D T1-weighted fast spoiled gradient echo sequence, on
1.5T Siemens scanner.
30

One can see granularities in the lesion and differences
between tissues due to the contrast dynamics illustrated
in figure 5(a) that are not seen on the corresponded
subtracted image of figure 5(b). Comparison of these

characteristics   with   ones   of   the   anatomically
identifiable tissues is used for understanding of the
structure of the lesion.   Figure 5(c) shows zoomed first
image of the sequence of processed post-contrast images

5   presented in figure 5(a).   The dark area at the top of
the   lesion   (pointed   by   the   white   arrow)   was   later
identified as a blood vessel. The dark area at the centre
(black   arrow)   is   a   compact   region   (shape   has   been
assessed using an orthogonal display), and therefore most

10   likely is part of the tumour that becomes enhanced later
than the surrounding tissue.

Figures 6(a) and (b) show another example of an image
processed according to the present invention (figure

15   6(a)) and one generated by simple subtraction of datasets
(figure 6(b)).   In figure 6(a) one can see a dark region
in the middle of the lesion. This non-homogeneity is not
seen on the corresponding subtracted image of figure
6(b). The method was initially valuated using 24 studies.

20   In all the cases the approach has been shown more
informative that the traditional subtracted image
technique. Suppression of the ill-effects of fat upon a
contrast-enhancement image significantly reduces the
amount of data to be analysed. This results in faster and

25   more reliable localisation of lesion, and the tumour
contour is clearly defined. The method provides a
capability of fast visual and reliable analysis of the
data that is otherwise available only from analysis of
individual uptake curves. Visualisation of differences in

30   the dynamic contrast characteristics of the tissue
provides a way for discrimination between tumour and
blood vessels, and identification of granularities.

The complete elimination of the fatty tissue surrounding the lesion identifies the tumour's contour clearly, and provides a straightforward way for segmenting tumour extent and extracting features.

5

A further example of the present invention shall now be described.

Effective fat suppression in images is of major
10 importance for dynamic contrast enhanced MRI of the breast. Current approaches rely on subtraction, fat saturation or water excitation. Selective saturation or excitation require high field uniformity that can often present a challenge. Subtraction imaging will not
15 completely remove fat, since fatty tissue is enhancing to some small extent. In addition subtraction increases noise of resulted difference image, and as a result the tumour outline is not always well defined.

20 The following example of the invention provides a "fat suppression" method based on multivariate statistical analysis and modelling of individual voxel (or pixel) dynamic contrast agent uptake curves. That is to say, the following example method provides a method which enables
25 one to identify and remove from the image dataset the uptake curves that belong to fatty tissue. In addition, the method transforms the dynamic data into a new 4D dataset (one temporal dimension and three spatial dimensions) with maximised contrast between the enhancing
30 tissues and improved contrast for lesions. The method demonstrates capabilities of identification of a lesion's boundary or contour, inhomogeneities, and visualisation of spatio-temporal patterns of contrast enhancement on T1-weighted dynamic studies.

The method was applied to 16 Gd-DTPA dynamic studies acquired on 1.5 Tesla scanners using T1-weighted fast spoiled gradient echo sequence. In all the cases

5   anatomically correct fat suppression was observed comparing the results with corresponded subtracted and fat-saturated images.

The method provides a way of producing dynamic images

10 combining high spatial and temporal resolution with fat suppression. The method is robust to non-uniformity of the magnetic field and heterogeneities of tissues.

Dynamic contrast enhanced MRI (DCE-MRI) is an effective

15 tool for diagnosis of breast cancer. The diagnosis relies on a number of features including among others the lesion's shape and spatio-temporal pattern of contrast enhancement. Analysis of the shape can only be reliable if the lesion's extent is properly segmented.

20

Applying specific linear transformation to the uptake vectors, the current approach described herein improves contrast between tissues with different contrast enhancement dynamics. This provides a way of detecting

25 granularity in a lesion and discriminating between lesion and functional tissue. The approach operates on feature spaces of unlimited dimensions.

A dynamic dataset can be considered as a set of uptake

30 vectors $\mathbf{u}_i = \left(u_{i,1},...,u_{i,M}\right)^T$ each of those represents a time evolution of signal intensity of a voxel at specific spatial location denoted by the index $i = 1,...,N$ through the sequence of M consecutively acquired volumes (i.e. an

intensity uptake curve of the i-th voxel), and $(\ )^T$ denotes transpose operation (vectors will be considered as column vectors.)

5   We assume that each uptake vector belongs to a certain cluster or group of such vectors possessing multivariate normal distribution. The members of the same cluster possess physiologically the same uptake curve form and the observed differences with the cluster are only due to

10   the random noise. Assuming that values of white noise at different time points of the same uptake curve are uncorrelated and equivalently distributed, the scatter within the clusters is assumed isotropic. Because of effects of heterogeneity of the tissues and non-

15   uniformity of magnetic field, each tissue will be represented by a number of such clusters. It is assumed that those factors affect the signal in fat by a spatial location specific multiplier. Thus the mean vectors of the clusters representing the fatty tissue will be

20   collinear:

$$\boldsymbol{\mu}_k = H_k \cdot \boldsymbol{\mu}_F , \quad k = 1,2,\ldots \tag{5}$$

There H_k is a multiplying factor, and $\boldsymbol{\mu}_F$ is a normalized

25   to unit length vector denoting the direction, shared by the mean vectors $\boldsymbol{\mu}_k = \left(\mu_{i,1},\ldots,\mu_{i,M}\right)^T$ of the fat clusters (hereafter $\boldsymbol{\mu}_F$ will be referred to as normalized signature vector of fat). If the vector $\boldsymbol{\mu}_F$ is known (its estimation will be discussed below), the following linear

30   transformation will create a new feature space where the mean vectors of the fat clusters are aligned with the zero vector:

$$\mathbf{v}_i = \mathbf{u}_i - (\mathbf{\mu}_F, \mathbf{u}_i) \cdot \mathbf{\mu}_F = (\mathbf{E} - \mathbf{\mu}_F \cdot \mathbf{\mu}_F^T) \cdot \mathbf{u}_i, \qquad i = 1, \dots N \qquad (6)$$

where $(\mathbf{\mu}_F, \mathbf{u}_i)$ denotes dot product, and $\mathbf{E}$ is the identity
matrix. Applying expectation operator to eq. 6 and then
5   substituting $\mathbf{\mu}_k$ according to eq. 5, one can show that the
expectation of a feature vector $\mathbf{v}_i$ is a zero-vector if
the corresponding uptake vector $\mathbf{u}_i$ belongs to one of the
clusters representing fat. Hereafter the vectors $\mathbf{u}_i$ will
be referred to as original uptake vectors, and $\mathbf{v}_i$ — as
10   residual uptake vectors.

The transform defined by eq. 6 can be interpreted
geometrically as subtraction from each original uptake
vector of its projection on the axis defined by the
15   normalized signature vector of fat $\mathbf{\mu}_F$. It follows that
the transform matrix $\mathbf{E} - \mathbf{\mu}_F \cdot \mathbf{\mu}_F^T$ is singular and its rank
(and therefore the dimension of the new feature space) is
$M - 1$. According to the above discussion, the residual
uptake vectors of fat will posses a single cluster with
20   zero mean vector and isotropic scatter. The residual
uptake vectors of non-fatty tissues will demonstrate
differences in contrast agent uptake dynamics as compared
to the fat, and will obviously possess significantly non-
Gaussian mixture of multivariate distributions.
25

To discriminate the feature vectors of fat and non-fatty
tissues, one may apply principal component analysis
(PCA). PCA will search for a new orthogonal basis in the
space of residual uptake vectors maximizing consecutively
30   variance of the projections on each of the axes. Since
the residual uptake vectors of fat have normal
distribution with zero mean vector and isotropic scatter,

their contribution to the total variance of the projections will be isotropic, and for any axis, the projections of the residual vectors of fat will possess normal distribution with zero mean. Thus the search will

5   be driven by variability of the residual uptake vectors of the tissues other than fat. The first (i.e. the most significant) principal component accounts for the most variability in the data, and, therefore, it will be maximally associated with the differences between fat and

10   non-fatty tissues.

The eigenimage of the first principal component (i.e. an image whose voxels/pixels are values of the first principal component of the corresponded residual uptake

15   vectors) will visualise differences in effect of contrast enhancement between fat and other tissues, and the fatty tissue on this image will be presented as a random noise with zero mean.

20   Fitting the model normal distribution as shown in Fig. 7, decomposes the distribution of values of the first principal components into a Gaussian fraction modelling the cluster of fatty tissue, and the residual non-Gaussian fraction. Applying receiver operation

25   characteristic (ROC) analysis, the optimal threshold discriminating the fractions is found. Finally, using this threshold, a mask of fatty tissue is created and used for elimination of fatty tissue from the images by performing a masking operation.

30

The mask will be a binary image of the same lattice dimensions as the original images where i-th voxel will be substituted by value 1, if the vector v_i was classified as representing non-fatty tissue, and zero

otherwise. The operation of masking mentioned above is, therefore, voxel wise multiplication of an image and the mask. The optimal threshold can also be found interactively adjusting the threshold and simultaneously

5 observing that no important details are cut off on the eigenimage.

Fig. 7 illustrates a histogram of the values of first principal components of the residual uptake vectors (the

10 data is from one of the examples discussed later). The Gauss curve modelling the fat cluster in the feature space is fitted varying mean and standard deviation of the Gauss curve and the weight of Gaussian fraction in the mixture.

15

Perfusion of fat is much slower than of the other tissues, and typical dynamic measurement shows only the beginning of the distribution phase terminating long before the equilibrium. At these conditions, we will

20 consider enhancement of fat as approximately linear, i.e. μ_F will be approximated as a linear function of time post contrast agent administration:

$$\mu_{F_j} = A \cdot \left(1 + r \cdot t_j\right), \qquad j = 1,...,M \tag{7}$$

25

where r is relative rate of enhancement of signal in fat due to the contrast agent, t_j - time of acquisition of the j-th volume measured since contrast agent administration, and A is a constant normalizing the vector to unit

30 length. The following iterative procedure is used to estimate the rate of enhancement r. Applying increasing values of r, starting from $r = 0$, the transformation defined by eq. 6 is computed followed by PCA of the

residual uptake vectors. Then the Gauss model is fitted
as discussed above. Finally, the accepted value of the
parameter is one resulting in the Gauss curve with the
centroid point closest to the zero.

5

PCA is known as a good tool to find axes separating
mixtures of multivariate Gaussian distributions. The PCA
applied to the uptake vectors before performing the
transform defined by the eq. 6 will outline the axis μ_F.

10

It was found that the first (i.e. the most significant)
principal component of the uptake vectors is very close
to μ_F, and can be used as its rough estimate of (Fig.
8). The most significant of the remaining principal

15 components (in this case the second) may be used as an
axis for discriminant analysis. This principal component
vector is identified as one possessing the smallest angle
with the identity vector (a vector of equal values).

20 The method can be combined with PCA based approached for
noise reduction by reconstructing the uptake vectors back
from their principal components values discarding non-
significant principal components.

25 Figure 8 illustrates the result of three different
estimation methods for estimating the normalized
signature vector of fat: solid line - linear model;
dotted - first principle component vector of the original
uptake vectors; dashed - average uptake curve of ROI

30 selected within fatty tissue (ROI size - 100 voxels),
this last method is crude and it is shown only for the
purpose of comparison.

The present approach was applied to 16 dynamic studies of
patients at genetic risk of breast cancer. Each study
consists of two pre-contrast and at least four post-
5   contrast datasets acquired using a 3D T1-weighted fast
spoiled gradient echo (FLASH) sequence with TE = 10-14
ms, TR = 4.2-5 ms, and flip angle - 35° on 1.5T scanners
of various models (mainly Siemens Magnetom and GE Signa).
The contrast agent was Gd-DTPA administrated by
10   intravenous bolus injection. Temporal resolution was 90
sec. in most cases. Image stack plane orientation was
coronal, with the matrix size 256x128 voxels and
corresponding spatial resolution 1.33x1.33 mm. Number of
slices was 64 to 60, and slice thickness 2.5 mm. As part
15   of the study protocol, 3D T1-weighted fat-saturated image
was acquired using similar sequence with higher spatial
resolution 0.66x0.89 mm (matrix size 512x384).

The data was previously checked for motion, and the
20   background was segmented applying threshold on length of
the uptake vectors. For each case a mask of fat tissue
was computed as discussed. To verify the correctness of
the method, the mask was applied to subtraction image,
and the result was compared with the original (i.e.
25   unmasked) subtraction image. In all the cases
anatomically correct fat suppression was observed. The
normalized signature vector of fat was computed both
using iterative algorithm and PCA of the original uptake
vectors. In both cases similar mask images were obtained.
30   The values of parameter r of eq. 7 were in the range
0.1-0.15.

Finally the computed mask was applied to the dataset of
residual uptake vectors. It was found that the produced

images have improved contrast for enhancing lesions comparing to the subtracted images. Here we present two examples.

5   Figures 9(a) to 9(f) and figures 10(a) to 10(d) present a study of a patient with invasive carcinoma (mixed lobular and no specific type (ductal) carcinoma, grade II.) Examples using the data of this study were demonstrated earlier (Fig. 7 and 8).

10

Fig.9(a) illustrates a subtracted image of a dataset acquired at 450 sec post contrast agent administration after applying fat mask and de-noising using PCA; Fig.9(b) illustrates the

15   original subtracted image; Fig.9(c) illustrates the difference image of (a) and (b). For further comparison there is illustrated: Fig.9(d) shows high resolution image with fat saturation (spatial resolution 0.66x0.89x2.5 mm); Fig9(e) shows an

20   eigenimage of the 1st principal component of the feature vectors; and Fig9(f) shows a computed binary mask of fatty tissue.

The lesion is shown by arrow on Fig.9(a).

25

In Fig.10(a)-(d) is shown a sequence of post-contrast images after transformation according to the eq. 7 and fat bit masking Figs.10(a,b), and corresponding sequence of subtracted images Figs.10(c,d). Post-administration

30   time is printed on the images. The lesion is boxed in all the images. Comparing the sequences one can see anatomically correct fat suppression. The backgrounds of the Figs.10(a,b) vary since the images contain signed values, and the background grey colour corresponds to the

value of zero that outlines the suppressed (i.e. masked out) fat. One can see granularity of the lesion better than it is seen on the corresponded subtracted images. Comparison of these characteristics with ones of the

5   anatomically   identifiable   tissues   is   used   for understanding of the structure of the lesion. The dark area at the top of the lesion (pointed by the white arrow) was identified as a blood vessel. The dark area at the centre (black arrow) is a compact region (shape has

10   been assessed using an orthogonal display), and therefore most likely is part of the tumour that becomes enhanced later than the periphery, that is seen comparing the images 10(a) and 10(b).

15   Figures 11(a) to 11(c) demonstrate another study of a patient with invasive ductal carcinoma (grade II). Comparing to the previous example, this example demonstrates denser parenchyma, and therefore of interest. Both studies were acquired using Siemens

20   Magnetom scanner.

     Figs. 11(a) and 11(b) illustrate a sequence of processed images. The lesion is in the left breast (shown by arrow). Ring type enhancement is clearly

25   demonstrated comparing the images. Figure 11(c) is provided for further comparison and was obtained at higher resolution T1 weighted image with fat saturation.

30   Elimination of fatty tissue from the dynamic dataset significantly reduces the amount of data to be analysed, and suggested linear transformation of the dataset improves contrast for functional and lesion tissues. This may result in faster and more reliable localisation of

lesion, and the tumour contour is clearly defined. Visualisation of differences in the dynamic contrast characteristics of the tissue enables analysis of spatio-temporal pattern of contrast enhancement, identification

5   of lesion's granularity and discrimination between lesion and attached healthy tissues (e.g. blood vessels). In the cases when lesion is surrounded by fatty tissue, the complete elimination of fat identifies the tumour's contour clearly, and provides a straightforward way for

10 segmenting tumour extent and feature extraction.

The method provides a classification tool, which is robust to tissue heterogeneity and non-uniformity of magnetic field. Also the method does not require feature

15 space dimension reduction (other existing clustering approaches operate on 3D feature spaces.)

The method has been described in terms of Breast MR imaging. However, it can be applied to other types of

20 dynamic MR studies as will be readily apparent to the skilled person. Modifications and variants to the above embodiments, such as would be readily apparent to the skilled person, are encompassed within the scope of the present invention.

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